

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
26 May 2005 (26.05.2005)

PCT

(10) International Publication Number
WO 2005/047463 A3

(51) International Patent Classification:
C12Q 1/70 (2006.01) *A61K 39/145* (2006.01)

(74) Common Representative: **MERCK & CO., INC.**; 126 East Lincoln Avenue, Rahway, New Jersey 07065-0907 (US).

(21) International Application Number:
PCT/US2004/036575

(22) International Filing Date:
3 November 2004 (03.11.2004)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/517,605 5 November 2003 (05.11.2003) US

(71) Applicants (for all designated States except US):
MERCK & CO., INC. [US/US]; 126 East Lincoln Avenue, Rahway, New Jersey 07065-0907 (US). **ISTITUTO DI RICERCHE DI BIOLOGIA MOLECOLARE P. ANGELETTI SPA.** [IT/IT]; Via Pontina KM. 30, 600, I-00040 Pomezia (IT).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **LUDMERER, Steven, W.** [US/US]; 126 East Lincoln Avenue, Rahway, New Jersey 07065-0907 (US). **GRAHAM, Donald, J.** [US/US]; 126 East Lincoln Avenue, Rahway, New Jersey 07065-0907 (US). **LAFFEMINA, Robert, L.** [US/US]; 126 East Lincoln Avenue, Rahway, New Jersey 07065-0907 (US). **FLORES, Osvaldo, A.** [CL/US]; 126 East Lincoln Avenue, Rahway, New Jersey 07065-0907 (US). **PIZZUTI, Maura** [IT/IT]; Via Pontina KM. 30, 600, I-00040 Pomezia (IT). **TRABONI, Cinzia** [IT/IT]; Via Pontina KM. 30, 600, I-00040 Pomezia (IT).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

— with international search report

(88) Date of publication of the international search report:
12 July 2007

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: HCV REPLICONS CONTAINING NSSB FROM GENOTYPE 2B

SMSYZ¹WTGALITPCGP EEEKLP I X¹PLSN S L X²RFHNKVYSTTSRSASLR AKKVTFDRVQV
LDAH YDSVLQDV KRAASKVSARLLTVEEACALTPPHSAK SRYGFGAKEVRSLSRRAVNHIR
SVWEDLLEDQHTPIDTTIMAKNEVFCIDPTKGGKKPARLIVYPDLGVRVCEKMALYDIAQK
LPKAIMGPSYGFQYSPAERVDFLLKAWGSKKDPMGFSYDTRCFDSTVTERDIRTEESIYQA
CSLPQEARTVIHSLTERLYVGGPMTNSKGQSCGYRRCRASGVFTTSMGNTMTTCYIKALAAC
KAAGIVDPVMLVCGDDL VVISESQGNEEDERNLRAFTEAMTRY SAPP GDLPRPEYDLELIT
SCSSNV SVALDSRGRRRYFLTRDPTTP X³TRAAWETVRHSPVNSWLGNIIQYAPTIVWRMVI
MTHFFSILLAQDTLNLQNLNFEMYGAVYSVNPLDLPATIERLHGLEAFSLHTYSPHELSRVA
ATLRKLGAPPLRAWKSRARAVRASLIAQGARA AICGRYLFNWAVKTKLKLTPLEASRLDL
SGWFTVGAGGGDIYHSVSHARPRL LLLCLLLLSVGVGIFLLPDR

(57) Abstract: The present invention features methods for enhancing the ability of a genotype 2b NS5B sequence to function in a replicon, for producing replicons containing a functional genotype 2b NS5B, and for using replicons to measure the ability of a compound to affect HCV replication that is sustained with the genotype 2b polymerase. Also featured is a genotype 1b NS4B adaptive mutation. The ability to produce replicons containing a functional genotype 2b NS5B is illustrated by the production of chimeric replicons based on HCV genotype 1b where substantially all the NS5B sequence is replaced with a genotype 2b NS5B.

WO 2005/047463 A3